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(FILE 'HOME' ENTERED AT 16:17:46 ON 21 JUL 2004)

L1 FILE 'HCAPLUS' ENTERED AT 16:17:57 ON 21 JUL 2004  
1 US20040034096/PN

FILE 'REGISTRY' ENTERED AT 16:18:18 ON 21 JUL 2004

L2 FILE 'HCAPLUS' ENTERED AT 16:18:21 ON 21 JUL 2004  
TRA L1 1- RN : 45 TERMS

L3 FILE 'REGISTRY' ENTERED AT 16:18:21 ON 21 JUL 2004  
45 SEA L2

L4 FILE 'WPIX' ENTERED AT 16:18:23 ON 21 JUL 2004  
1 US20040034096/PN

=> b hcap

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FILE COVERS 1907 - 21 Jul 2004 VOL 141 ISS 4  
FILE LAST UPDATED: 20 Jul 2004 (20040720/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L1 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2004:60452 HCAPLUS  
DN 140:128156  
ED Entered STN: 26 Jan 2004  
TI Preparation of cinnamide derivatives useful as selective MAO-B inhibitors  
IN Jolidon, Synese; Rodriguez, Sarmiento Rosa Maria; Thomas, Andrew William;  
Wostl, Wolfgang; Wyler, Rene  
PA F. Hoffmann-La Roche AG, Switz.  
SO PCT Int. Appl., 28 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM C07C235-34  
ICS C07C255-54; A61K031-165; A61K031-275; A61P025-28  
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Searched by Noble Jarrell

Section cross-reference(s): 1, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004007429	A1	20040122	WO 2003-EP7231	20030707
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2004034096	A1	20040219	US 2003-613785	20030703 <--
PRAI	EP 2002-15583	A	20020715		
OS	MARPAT 140:128156				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention refers to cinnamide derivs. of formula I [wherein: R1 = alkyl, halogen, halogenoalkyl, CN, alkoxy, halogenoalkoxy; R21, R22, R23, R24 = H or F; R3 = H, alkyl; A = -C(R4):C(R5)-, -C(R4)(R6)-C(R7)(R5)-, or -C.tplbond.C-; R4, R5, R6, R7 = H, alkyl; n = 1-3] useful for treatment and prevention of diseases mediated by MAO-B inhibitors. Compds. I are especially useful for the treatment of Alzheimer's disease and senile dementia. For instance, compound II (example 1, IC50 = 0.083 .mu.mol for human MAO-B; >10,000 for human MAO-A) was prepared via etherification of 4-iodophenol by 3-fluorobenzyl bromide, Sonogashira reaction of CH2:C(Me)CO2Me with obtained compound III, subsequent hydrolysis and amidation.

ST cinnamide prepn MAO monoamine oxidase inhibitor

IT Anti-Alzheimer's agents

Human

(preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT Mental disorder

(senile psychosis, treatment of; preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT Alzheimer's disease

(treatment of; preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 9001-66-5

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(B, inhibitors, mediated diseases; preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 649740-30-7P, 1-(3-Fluorobenzoyloxy)-4-iodobenzene 649740-31-8P, 3-[4-(3-Fluorobenzoyloxy)phenyl]-2-methylacrylic acid methyl ester 649740-32-9P, 3-[4-(3-Fluorobenzoyloxy)phenyl]-2-methylacrylic acid

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 649740-29-4P, 3-[4-(3-Fluorobenzoyloxy)phenyl]-2-methylacrylamide 649740-33-0P, 3-[4-(3-Fluorobenzoyloxy)phenyl]-2,N-dimethylacrylamide 649740-53-4P, 3-[4-(3-Fluorobenzoyloxy)phenyl]but-2-enoic acid methylamide

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 649740-34-1P, 3-[4-(3-Fluorobenzoyloxy)phenyl]-2-methylpropionamide  
 649740-35-2P, 3-[4-(3-Fluorobenzoyloxy)phenyl]-2,N-dimethylpropionamide  
 649740-36-3P, 3-[4-(3-Fluorobenzoyloxy)phenyl]propynoic acid amide  
 649740-40-9P, 1-[4-(3-Fluorobenzoyloxy)phenyl]propynoic acid methylamide  
 649740-41-0P, 3-[4-(3,4-Difluorobenzoyloxy)phenyl]propionamide  
 649740-42-1P, 3-[4-(3-Fluorobenzoyloxy)phenyl]-N-methylacrylamide  
 649740-45-4P, 3-[4-(3-Fluorobenzoyloxy)phenyl]acrylamide 649740-46-5P,  
 N-Methyl-3-[4-(4-trifluoromethylbenzoyloxy)phenyl]acrylamide  
 649740-47-6P, 3-[4-(3,4-Difluorobenzoyloxy)phenyl]-N-methylacrylamide  
 649740-49-8P, 3-[4-(4-Fluorobenzoyloxy)phenyl]-N-methylacrylamide  
 649740-50-1P, 3-[4-(3-Cyanobenzoyloxy)phenyl]-N-methylacrylamide  
 649740-51-2P, N-Methyl-3-[4-(4-methylbenzoyloxy)phenyl]acrylamide  
 649740-52-3P, 3-[4-(3-Methoxybenzoyloxy)phenyl]-N-methylacrylamide  
 649740-55-6P, 3-[4-(3-Fluorobenzoyloxy)phenyl]-N-methylbutyramide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 93291-55-5P, 1-[4-(3-Fluorobenzoyloxy)phenyl]ethanone 94530-63-9P,  
 3-(4-Hydroxyphenyl)-N-methylacrylamide 175136-19-3P,  
 3-[4-(4-Fluorobenzoyloxy)phenyl]acrylic acid 423752-10-7P,  
 3-[4-(3-Fluorobenzoyloxy)phenyl]acrylic acid 649740-37-4P,  
 [[4-(3-Fluorobenzoyloxy)phenyl]ethynyl]-trimethylsilane 649740-38-5P,  
 1-(3-Fluorobenzoyloxy)-4-ethynylbenzene 649740-39-6P,  
 [4-(3-Fluorobenzoyloxy)phenyl]propynoic acid 649740-43-2P,  
 3-[4-(3-Fluorobenzoyloxy)phenyl]acrylic acid 3-fluorobenzyl ester  
 649740-44-3P, 3-[4-(3-Fluorobenzoyloxy)phenyl]acryloyl chloride  
 649740-48-7P, 3-[4-(3,4-Difluorobenzoyloxy)phenyl]acrylic acid  
 649740-54-5P, 3-[4-(3-Fluorobenzoyloxy)phenyl]but-2-enoic acid methyl ester  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 80-62-6, Methyl methacrylate 99-93-4, 4-Hydroxyacetophenone 104-81-4,  
 1-Bromomethyl-4-methylbenzene 402-49-3, 4-(Trifluoromethyl)benzyl  
 bromide 456-41-7, 3-Fluorobenzyl bromide 459-46-1, 4-Fluorobenzyl  
 bromide 540-38-5, 4-Iodophenol 874-98-6, 1-Bromomethyl-3-  
 methoxybenzene 1066-54-2, Trimethylsilylacetylene 7400-08-0, p-Cumaric  
 acid 23838-70-2, 3-(4-Hydroxyphenyl)propionamide 28188-41-2,  
 3-Bromomethylbenzonitrile 85118-01-0, 3,4-Difluorobenzyl bromide  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; preparation of cinnamide derivs. useful as MAO-B inhibitors)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
 (1) Bentue-Ferrer, D; CNS DRUGS 1996, V6(3), P217 HCAPLUS  
 (2) Fournier Innovation Synergie; WO 9011997 A 1990 HCAPLUS  
 (3) Rano, T; TETRAHEDRON LETTERS 1995, V36(22), P3789 HCAPLUS

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FILE 'WPIX' ENTERED AT 16:19:02 ON 21 JUL 2004  
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FILE LAST UPDATED: 20 JUL 2004 <20040720/UP>  
 MOST RECENT DERWENT UPDATE: 200446 <200446/DW>  
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> THE DISPLAY LAYOUT HAS BEEN CHANGED TO ACCOMMODATE THE  
 NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION  
 NUMBERS. SEE ALSO:  
<http://www.stn-international.de/archive/stnews/news0104.pdf> <<<

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L4 ANSWER 1 OF 1 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 2004-191103 [18] WPIX  
 DNC C2004-075334  
 TI New cinnamide derivatives are monoamine oxidase B inhibitors useful for  
 treating e.g. Alzheimer's disease and senile dementia.  
 DC B05  
 IN JOLIDON, S; RODRIGUEZ SARMIENTO, R M; THOMAS, A W; WOSTL, W; WYLER, R  
 PA (JOLI-I) JOLIDON S; (SARM-I) RODRIGUEZ SARMIENTO R M; (THOM-I) THOMAS A W;  
 (WOST-I) WOSTL W; (WYLE-I) WYLER R; (HOFF) HOFFMANN LA ROCHE & CO AG F  
 CYC 101  
 PI WO 2004007429 A1 20040122 (200418)\* EN 28 C07C235-34  
 RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS  
 LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
 RO RU SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW  
 US 2004034096 A1 20040219 (200418) A61K031-277 <--  
 ADT WO 2004007429 A1 WO 2003-EP7231 20030707; US 2004034096 A1 US 2003-613785  
 20030703  
 PRAI EP 2002-15583 20020715  
 IC ICM A61K031-277; C07C235-34  
 ICS A61K031-165; A61K031-275; A61P025-28; C07C255-54  
 AB WO2004007429 A UPAB: 20040316  
 NOVELTY - Cinnamide derivatives are new.  
 DETAILED DESCRIPTION - Cinnamide derivatives of formula (I) are new.  
 R1 = 1-3C alkyl, halo, halo-(1-6C)alkyl, cyano, 1-6C alkoxy or  
 halo-(1-6C)alkoxy;  
 R21-R24 = H or F;  
 R3, R4 = H or 1-3C alkyl;  
 A = C(R4)=C(R5), C(R4)(R6)-C(R5)(R7) or C triple bond C;  
 R5-R7 = H or 1-6C alkyl, and  
 n = 1-3.  
 An INDEPENDENT CLAIM is also included for the preparation of (I).  
 ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian;  
 Antidepressant; Tranquilizer; Neuroleptic; Eating-Disorders-Gen.;  
 Anorectic; Antiaddictive; Antismoking; Antiinflammatory.  
 MECHANISM OF ACTION - Monoamine oxidase B inhibitor.  
 The monoamine oxidase B enzymatic activity of 3-(4-(3-

fluorobenzyloxy)-phenyl)-2,N-dimethyl-propionamide (Ia) was assayed in 96-well-plates using a spectrophotometric assay adapted from the method as described in Zhou and Panchuk-Voloshina (A One-Step Fluorometric Method for the Continuous Measurement of Monoamine Oxidase Activity, Analytical Biochemistry 253:169-174 (1997)). The IC50 value of (Ia) was 0.029 micro mol.

USE - Used for treatment and prevention of Alzheimer's disease and senile dementia (claimed), acute and chronic neurological disorder, cognitive disorder, memory deficit, dementia, minimal cognitive impairment, Parkinson's disease, psychiatric diseases (e.g. depression, anxiety, panic attack, social phobia, schizophrenia, eating and metabolic disorder (e.g. obesity)), withdrawal symptoms induced by abuse of alcohol, nicotine and other addictive drugs and other neuroinflammatory diseases.

Dwg.0/0

FS CPI  
FA AB; GI; DCN  
MC CPI: B10-A15; B10-D03; B14-C03; B14-D05C; B14-E11; B14-E12; B14-J01;  
B14-M01

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